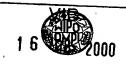


PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7: C07K 14/54, 14/715

A3

(11) International Publication Number:

WO 00/23471

(43) International Publication Date:

27 April 2000 (27.04.00)

(21) International Application Number:

PCT/EP99/07800

(22) International Filing Date:

6 October 1999 (06.10.99)

(30) Priority Data:

98203529.7

20 October 1998 (20.10.98) El

EP

(71) Applicant (for all designated States except US): VLAAMS INTERUNIVERSITAIR INSTITUUT VOOR BIOTECH-NOLOGIE VZW [BE/BE]; Rijvisschestraat 120, B-9052 Zwijnaarde (BE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): STEIDLER, Lothar [BE/BE]; Bokslaarstraat 41, B-9160 Lokeren (BE). REMAUT, Erik, Rene [BE/BE]; Bergstraat 7, B-9921 Vinderhoute (BE). FIERS, Walter [BE/BE]; Beukendreef 3, B-9070 Destelbergen (BE).

(74) Common Representative: VLAAMS INTERUNIVERSITAIR INSTITUUT VOOR BIOTECHNOLOGIE VZW; Rijvisschestraat 120, B-9052 Zwijnaarde (BE).

(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

With international search report.

(88) Date of publication of the international search report:

3 August 2000 (03.08.00)

(54) Title: USE OF A CYTOKINE-PRODUCING LACTOCOCCUS STRAIN TO TREAT COLITIS

(57) Abstract

The current invention relates to an administration strategy for the delivery at the intestinal mucosa of cytokines or cytokine antagonists, preferably of acid sensitive anti-inflammatory agents, such as IL10 and/or soluble TNF receptor via the oral route. The prefered feature according to the invention is the inoculation with a suspension of recombinant *Lactococcus lactis* cells, which had been engineered to produce the respective proteins.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

| AL | Albania | ES | Spain | LS | Lesotho | SI | Slovenia |
|----|--------------------------|----|---------------------|----|-----------------------|-----|-------------------------|
| AM | Armenia | FI | Finland | LT | Lithuania | SK | Slovakia |
| ΑT | Austria | FR | France | LU | Luxembourg | SN | Senegal |
| ΑU | Australia | GA | Gabon | LV | Latvia | SZ | Swaziland |
| ΑZ | Azerbaijan | GB | United Kingdom | MC | Monaco | TD | Chad |
| BA | Bosnia and Herzegovina | GE | Georgia | MD | Republic of Moldova | TG | Togo |
| BB | Barbados | GH | Ghana | MG | Madagascar | T.J | Tajikistan |
| BE | Belgium | GN | Guinea | MK | The former Yugoslav | TM | Turkmenistan |
| BF | Burkina Faso | GR | Greece | | Republic of Macedonia | TR | Turkey |
| BG | Bulgaria | HU | Hungary | ML | Mali | TT | Trinidad and Tobago |
| BJ | Benin | IE | Ireland | MN | Mongolia | ÜA | Ukraine |
| BR | Brazil | IL | Israel | MR | Mauritania | UG | Uganda |
| BY | Belarus | IS | Iceland | MW | Malawi | US | United States of Americ |
| CA | Салада | IT | Italy | MX | Mexico | UZ. | Uzbekistan |
| CF | Central African Republic | JP | Japan | NE | Niger | VN | Viet Nam |
| CG | Congo | KE | Kenya | NL | Netherlands | YU | |
| CH | Switzerland | KG | Kyrgyzstan | NO | Norway | ZW | Yugoslavia |
| CI | Côte d'Ivoire | KP | Democratic People's | NZ | New Zealand | ZW | Zimbabwe . |
| CM | Cameroon | | Republic of Korea | PL | Poland | | |
| CN | China | KR | Republic of Korea | PT | Portugal | | |
| CU | Cuba | KZ | Kazakstan | RO | Romania | | |
| CZ | Czech Republic | LC | Saint Lucia | RU | Russian Federation | | |
| DE | Germany | Li | Liechtenstein | SD | Sudan | | |
| DK | Denmark | LK | Sri Lanka | SE | | | |
| EE | Estonia | LR | Liberia | SG | Sweden Singapore | | |

INTERNATIONAL SEARCH REPORT

ional Application No

PCT/EP 99/07800 CLASSIFICATION F SUBJECT MATTER C 7 C07K14/54 C07k C07K14/715 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 7 CO7K C12N Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. WO 96 11277 A (DOMPE SPA ; TAGLIABUE ALDO (IT); BORASCHI DIANA (IT); BOSSU PAOLA () X 1-6 18 April 1996 (1996-04-18) page 2, line 6 - line 11; claims 1-6,8 page 4, line 22 - line 27 page 6, line 29 -page 7, line 6 page 10, line 2 -page 11, line 20 page 11, line 28 -page 12, line 2 page 13, line 25 -page 15, line 2 A WO 97 14806 A (UNIV CAMBRIDGE TECH 1-5 ;STEIDLER LOTHAR (BE); REMAUT ERIK (BE); WELLS) 24 April 1997 (1997-04-24) cited in the application page 8, line 22 -page 9, line 6; claims 1,7,8,12,18 page 11, line 19 - line 25 page 12, line 23 -page 13, line 27 Further documents are listed in the continuation of box C. X Patent family members are listed in annex. Special categories of cited documents : To later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone filing date "L" document which may throw doubts on priority claim(e) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-"O" document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled in the art. document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 20 April 2000 02/05/2000 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo ni, Fax: (+31-70) 340-3016

Charles, D

INTERNATIONAL SEARCH REPORT

Int. Jonal Application No PCT/FP 99/07800

| C/Continuation) DOCLIMENTS CONSIDERED TO BE RELEVANT | | | | | | |
|--|--|---------------------|--|--|--|--|
| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT Category Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. | | | | | | |
| | | Helevani to dam No. | | | | |
| A | STEIDLER L ET AL: "Mucosal delivery of murine interleukin-2 (IL-2) and IL-6 by recombinant strains of Lactococcus lactis coexpressing antigen and cytokine." INFECTION AND IMMUNITY, (1998 JUL) 66 (7) 3183-9. JOURNAL CODE: GO7. ISSN: 0019-9567., XP002105819 United States the whole document | 1,3,6 | | | | |
| | • | | | | | |
| | • | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |

INTERNATIONAL SEARCH REPORT

information on patent family members

Inti Jonal Application No PCT/EP 99/07800

| Patent document cited in search report | | Publication date | Patent family member(s) | | Publication dat | |
|--|---|------------------|-------------------------|------------|-----------------|--|
| WO 9611277 | Α | 18-04-1996 | IT | 1270123 B | 28-04-1997 | |
| | | | ΑÜ | 3745395 A | 02-05-1996 | |
| • | | | CA | 2201721 A | 18-04-1996 | |
| | | | EP | 0784689 A | 23-07-1997 | |
| | | | JP | 10506791 T | 07-07-1998 | |
| WO 9714806 | A | 24-04-1997 | AU | 7315496 A | 07-05-1997 | |
| | | | BR | 9610929 A | 21-12-1999 | |
| | | | CN | 1202934 A | 23-12-1998 | |
| | | | EP | 0871748 A | 21-10-1998 | |
| | | | NO | 981746 A | 22-06-1998 | |

IS PAGE BLANK (USPTO)